

**REMARKS**

Reconsideration of this application is respectfully requested. Claim 14 is pending for the Examiner's consideration.

**Rejection Under 35 U.S.C. § 103**

Claim 14 was rejected under 35 U.S.C. § 103 as obvious over U.S. 6,136,956 to Kogiso et al. or JP-B-3012932, also to Kogiso (both discussed collectively as "Kogiso") in view of U.S. Patent No. 6,743,638 to Tsilosani *et al.* ("Tsilosani") for the reasons discussed on pages 2-6 of the Office Action. Applicants respectfully traverse the rejection for the reasons that follow.

As noted in the previous amendment and response filed on July 20, 2007, Kogiso does not teach or suggest several limitations in pending claim 14, including, for example, a spherical microcapsule comprising a fine spherical body with a particle diameter of from 5  $\mu\text{m}$  to 15  $\mu\text{m}$ . Nor does Kogiso teach or suggest a microcapsule with uniform molecular orientation that when observed using a fluorescent microscope, emits fluorescence owing to pyranine as the inclusion compound.

Tsilosani describes utilizing a liposome as a stimuli-responsive microcapsule. See e.g., Tsilosani, col. 13, line 66 – col. 14, line 5. Liposome is a spherical self-organized matter containing a phospholipid as a constitutional molecule. It is defined as a simple model of a cell (membrane). The phospholipid, as a constitutional molecule, is a generalized amphipathic compound, an example of which includes phosphatidyl choline.

Liposome can be easily obtained by treating a suspension of a phospholipid. The production process thereof has been reported by Bangham *et al.* in the following reference documents:

A.D. Bangham and R.M.C. Dawson, Nature (1958) 182, 1292-1293

A.D. Bangham, Nature (1961) 192, 1197-1198

A.D. Bangham and R.W. Horne, Nature (1962) 196, 952-953.

As shown in "Intermolecular and Surface Forces" by J.N. Israelachvili, Academic Press, London, 1985, which is attached for the Examiner's convenience, there is a correlation between the forms of packing of amphipathic compounds and the structure formed by them. It is known that the phospholipid reported by Tsilosani forms a vesicle structure (liposome) owing to the

critical packing structure and the packing parameter thereof. See *id.*, wherein the critical packing shape is in the form of a truncated cone. In contrast, the compound of the present application has a critical packing structure in a cylindrical form, *i.e.*, the packing parameter is approximately "1". See *id.*, wherein the critical packing shape is in the form of a truncated cone. Therefore, it is expected to form only a planer molecular membrane, and one of skill in the art would not expect that it is capable of forming a vesicle structure which is a flexible molecular membrane. However, by analyzing in detail the mechanism of forming organized matter, the applicants found that the compound of the present application forms a vesicle structure as an intermediate, and further found that it can be produced as a spherical organized matter by subjecting it to an interaction with a surface-treated substrate.

In view of the above, one of ordinary skill in the art would have no reasonable expectation of success in combining the teachings of Kogiso and with those of Tsilosani to produce the claimed invention. Moreover, Tsilosani does not fill in the above-noted deficiencies of Kogiso, and thus a combination of the two references does not teach or suggest all of the claim limitations. For at least the reasons discussed above, applicants respectfully submit that claim 14 of the present invention is not obvious from the combination of Kogiso and Tsilosani.

Reconsideration with allowance is thus requested.

No additional fees are believed to be required for this submission. Should any fees be required, however, please charge those fees to Morgan, Lewis & Bockius LLP deposit account no. 50-0310.

Respectfully submitted,

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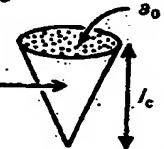


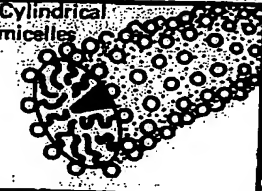

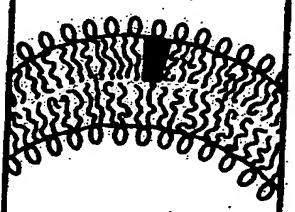

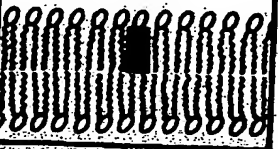

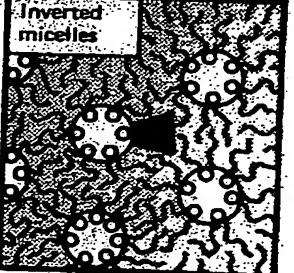
# "Intermolecular and Surface Forces"

by J. N. Israelachvili

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## CHAPTER 16. AGGREGATION OF AMPHIPHILIC MOLECULES

TABLE XXI  
Mean (dynamic) packing shapes of lipids and the structures they form

Lipid	Critical packing parameter $v/a_0 l_c$	Critical packing shape	Structures formed
Single-chained lipids (surfactants) with large head-group areas: <i>SDS in low salt</i>	$< 1/3$	Cone 	Spherical micelles 
Single-chained lipids with small head-group areas: <i>SDS and CTAB in high salt, nonionic lipids</i>	$1/3-1/2$	Truncated cone 	Cylindrical micelles 
Double-chained lipids with large head-group areas, fluid chains: <i>Phosphatidyl choline (lecithin), phosphatidyl serine, phosphatidyl glycerol, phosphatidyl inositol, phosphatidic acid, sphingomyelin, DGDG<sup>a</sup>, dihexadecyl phosphate, dialkyl dimethyl ammonium salts</i>	$1/2-1$	Truncated cone 	Flexible bilayers, vesicles 
Double-chained lipids with small head-group areas, anionic lipids in high salt, saturated frozen chains: <i>phosphatidyl ethanolamine, phosphatidyl serine + Ca<sup>2+</sup></i>	$\sim 1$	Cylinder 	Planar bilayers 
Double-chained lipids with small head-group areas, nonionic lipids, poly (cis) unsaturated chains, high T: <i>unsat. phosphatidyl ethanolamine, cardiolipin + Ca<sup>2+</sup>, phosphatidic acid + Ca<sup>2+</sup>, cholesterol, MGDG<sup>b</sup></i>	$> 1$	Inverted truncated cone or wedge 	Inverted micelles 

<sup>a</sup> DGDG, digalactosyl diglyceride, diglucosyl diglyceride; <sup>b</sup> MGDG, monogalactosyl diglyceride, monoglucosyl diglyceride.

Academic Press, London.

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